DETAILED ACTION

Comments

The preliminary amendment filed on 12 September 2005 is acknowledged and has been considered.

Election/Restrictions

Applicant's election without traverse of Species A (RNA) in the reply filed on 5 November 2009 is acknowledged.

However, the disclosed art also teaches Species C (protein/peptide). Consequently, in view of a lack of search burden between Species A and C, the species of protein/peptide is rejoined with the elected species of RNA.

Claims 1-26 are pending and examined in the instant Office action.

Information Disclosure Statement

The information disclosure statement filed on 12 September 2005 has been considered in part. Specifically, the reference of Perlin has not been considered because no date of publication is listed in the information disclosure statement or the publication itself.

Oath/Declaration

The declaration filed on 7 June 2006 is defective because all of the copies of the declaration do not list each inventor. In this instance, each copy of the declaration only includes a single inventor. See MPEP 201.03 II B and MPEP 605.04(a) for rules governing the signatures and listing of inventors on oaths and declarations submitted for an invention.

Specification

The abstract of the disclosure is objected to because the "sentence" is a fragment and not a full sentence (i.e. it lacks a verb). Correction is required. See MPEP § 608.01(b).

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Specifically, line 11 of page 10 discloses a hyperlink.

Claim Objections

Claim 1 is objected to because of the following informalities:

Line 2 of claim 1 recites "***an*** biomolecule sample," which should read "***a*** biomolecule sample."

Line 4 of claim 1 ends with a double colon wherein it should end with a single colon.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 4-5, 8, and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 is rejected because while the claim recites dependency from another claim, claim 16 does not list the identity of this specific claim. Consequently, it is not clear as to the metes and bounds of this claim. For the purpose of examination, it is interpreted that claim 16 depends from claim 15.

Claims 2, 4-5, and 8 recite a limitation regarding "anomalous cases." Absent a definition in the specification of the term, it is indefinite as to whether an anomalous case comprises artifacts on the electropherograms (i.e. Figures 8 and 9), potentially non-artifacts on the electropherogram (i.e. original claim 4), or either scenario. For the purpose of examination, anomalous cases are interpreted to broadly encompass either scenario.

Claim 4 is indefinite because while line 8 recites “the measured data,” it is unclear if this refers to “trial measured data" in line 4 or "measured data" in line 2 of claim 1. For the purpose of examination, this data is interpreted to refer to the latter.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following rejection is necessitated by applicant's amendments:

Claims 1-25 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-25 are drawn to a method or software program or product for determining the quality of a biomolecular sample.

This rejection is in line with the recent decision in *In re Bilski*, 545 F.3d 943, 88 USPQ2d 1385 (Federal Circuit, 2008). In the instant case, the claims are drawn to an abstract idea and therefore must be evaluated further for providing a practical application of the judicial exception. In order for a claim to provide a practical application, the claim **must meet** the machine-or-transformation test in order to be eligible under 35 USC 101 as statutory subject matter (*In re Bilski*, 545 F.3d 943, 88 USPQ2d 1385 (Federal Circuit, 2008). In other words, the prohibition on patenting abstract ideas has two distinct aspects: (1) when an abstract concept has no claimed practical application, it is not patentable; (2) while an abstract concept **may have a practical application,** a claim reciting an algorithm or abstract idea can state statutory subject matter only if it is embodied in, operates on, transforms, or otherwise is tied to another class of statutory subject matter under 35 U.S.C. §101 (i.e. a machine, manufacture, or composition of matter). (*Gottschalk v. Benson*, 409 U.S. 63, 175 USPQ 673, 1972), as clarified in *In re Bilski*, 545 F.3d 943, 88 USPQ2d 1385 (Federal Circuit,

2008) the test for a method claim is whether the claimed method is (1) tied to a particular machine or apparatus or (2) transforms a particular article to a different state or thing.

In the instant case, a physical transformation of matter is not provided, as the instant claims merely provide steps of information manipulation (i.e. extracting data, determining, collecting data, assigning data, specifying data). Therefore, none of said steps result in a physical transformation of matter such that the whole of the claim is statutory. For example, while claim 1 recites the use of "measured data" in the preamble, there is no active step of measuring data in the claim.

Further, the method claims (claims 1-24) are not so tied to another statutory class of invention because the **method** steps that are critical to the invention are "not tied to any **particular apparatus** or **machine**" and therefore do not meet the machine-or-transformation test as set forth in *In re Bilski* 545 F.3d 943, 88 USPQ2d 1385 (Federal Circuit, 2008).

It is noted that the preamble of claim 25 recites "a software program or product, PREFERABLY stored on a data carrier…" If this claim is interpreted to be a software program or product that is not on a data carrier, it is a program-- software and computer programs, per se, are not statutory. Even if the claim is interpreted to be on a data carrier, the term data carrier is only disclosed in the paragraph bridging pages 12-13 of the specification as "any type of data carrier." Consequently, data carriers are determined to encompass carrier waves, which are also not statutory.

It is noted that while instant claim 26 **IS** statutory because it is an apparatus (i.e. with structure) for processing data with a practical application of determining sample quality.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 8-9, 12, 15-16, 21-22, and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Carbeck et al. [Journal of the American Chemical Society, 1999, volume 121, pages 10671-10679].

Claim 1 is drawn to a method for determining the quality (using quality values of a biomolecular sample) based on data measured from the biomolecular sample. The method comprises extracting feature(s) from the data by data analysis and determining a quality value from the features using a quality algorithm. This quality algorithm involves collecting a statistically significant number of trial measured data covering a prescribed set of biomolecule samples and assigning a quality label to each measured data, extracting features from the data using analysis. The quality algorithm also comprises determining functional interrelations among the quality labels and one or more of the extracted features. The quality algorithm also comprises assigning a rating

factor to every functional interrelation and specifying the functional interrelation that has the highest rating factor as the quality algorithm.

The article of Carbeck et al. studies protein charge ladders derived using capillary electrophoresis. Specifically, electropherograms of protein mixtures are taken (such as in Figure 1A on page 10672 of Carbeck et al.) wherein the mixture is of the same generic protein molecule with varying numbers of amines acetylated. Since there is an integer distribution of the number of acetylated amines (wherein when an amine is acetylated, it cannot retain its positive charge), the electropherogram of the mixture (i.e. Figure 1A of Carbeck et al.) resembles a ladder wherein each "rung" has a different number of amines acetylated.

Consequently, Figure 1 of Carbeck et al. extracts a statistically significant number of trial measured data (i.e. the migration time for each rung of the ladder) which is converted according to equation 6 on page 10673 of Carbeck et al. to electrophoretic mobilities (i.e. the ordinate axis in Figure 1B of Carbeck et al.) A quality label is then assigned to each point of measured data using the abscissa of Figure 1B of Carbeck et al. (i.e. a value of $n\Delta Z_{seq}$). It is noted that the term “quality” is exemplified, but not defined, in the instant disclosure. In the absence of such a definition, the term quality is interpreted broadly to encompass the quality of electrostatic properties, such as $n\Delta Z_{seq}$.

The plots of Figure 1 of Carbeck et al. are used to determine the features of charge of the protein in the absence of acetylations (i.e. in Figure 1B of Carbeck et al., the x-intercept of the line tangent to the charge ladder data point "curve" at the curve’s y-intercept), and the mass and/or size of the protein (inversely proportional to the slope

of the above tangent line). Equations 7-9 on page 10673 of Carbeck et al. and equation 15 on page 10675 of Carbeck et al. list the functional interrelations between the quality labels and features (i.e. the electrophoretic mobilities, charge, mass, and radius) of the protein. Specifically, equation 15 on page 10675 of Carbeck et al. uses Debye-Huckel theory to determine the radius of the protein from electrostatic properties. When this functional interrelation is applied to the charge ladder data in Figure 3 of Carbeck et al., the best quality of agreement (i.e. rating or quality value) occurs when the radius of the protein is set to 2.1 nm [see Figure 3 of Carbeck et al. and the paragraph of text bridging pages 10675-10676 of Carbeck et al.].

With regard to claim 2, the anomalous cases in Figure 1A of Carbeck on page 10672 are interpreted to be the peaks specified with asterisks.

With regard to claim 3, Figure 3 of Carbeck et al. illustrates functions that are adaptively fit to the data by adapting or varying the value of the radius.

Claims 4-5 recite similar analyses than claim 1, except that it is applied to anomalous data. In view of the indefiniteness rejection above, the term anomalous case is interpreted to encompass both artifacts and other data. Consequently, as discussed above, Carbeck et al. is interpreted to teach the quality algorithm applicable to both data and anomalous cases. Figure 3 of Carbeck et al. illustrates functions that are adaptively fit to the data by adapting or varying the value of the radius.

With regard to claim 6, the discrete classes of Figure 1 of Carbeck et al. are the discrete rungs of the charge ladder wherein each discrete class is assigned a quality label in Figure 1B.

With regard to claim 8, each artifact in Figure 1A of Carbeck et al. is binary in that the artifact is assigned a value of unity (an asterisk) is it exists, and zero (i.e. no asterisk) in the absence of an artifact.

With regard to claim 9, the charge ladder in Figure 1A is subdivided into segments based on the number of acetylated amines (i.e. the first rung has no acetylated amines, the second rung has one acetylated amine, and so on...)

With regard to claim 12, Figure 1B of Carbeck et al. illustrates fitting data to a curve based on the slope and y-intercept of the interpolating straight line fitted to the points falling within the bounds of the segment.

With regard to claims 15-16, Figure 1 and its caption in Carbeck et al. teach that the line is fit to the first five points (or rungs) of the charge ladder. In other words, as each feature is added (up to a consecutive value of five) the quality label is maximized by adding points to which the line is fit. This list of five rungs is based on mutual information from the electropherogram.

With regard to claims 21-22, the charge ladder in Figure 1 of Carbeck is of the protein bovine carbonic anhydrase II.

With regard to claim 24, Figure 1A of Carbeck et al. is an electropherogram.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

35 U.S.C. 103 Rejection #1:

Claims 25 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carbeck et al. as applied to claims 1-6, 8-9, 12, 15-16, 21-22, and 24 above, and further in view of Allison et al. [Biophysical Journal, volume 68, 1995, pages 2261-2270] in view of Allison et al. [Macromolecules, 1992, volume 25, pages 3971-3978]. This second reference of Allison et al. is referred to as Allison et al. (1992) throughout this Office action.

Claim 25 is drawn to similar subject matter as claim 1, except as a software program or product.

Claim 26 is drawn to similar subject matter as claim 1, except as an apparatus.

Carbeck et al. teaches a method for determining quality value of the biomolecule sample, as discussed above.

Carbeck et al. does not teach software of computing apparatus for executing this method.

Allison et al. teaches the computational modeling of electrostatics of a protein (i.e. lysozyme). Specifically, Figures 4-6 on page 2267 of Allison et al. illustrate several modeling algorithms for determining the charge on lysozyme as a function of pH (wherein computationally changing pH is the computational equivalent of modifying degree of acetylation as it also computationally alters charge on the protein). However, Allison et al. does not teach software of a physical structural apparatus.

The article of Allison et al. (1992) does use computer and software for calculating electrostatics around a sphere. Specifically, the second full paragraph on column 1 on

page 3977 of Allison et al. (1992) teaches use of a Silicon Graphics 4D/380 computer and its CPU.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the quality determination method of Carbeck et al. by use of the computers in Allison et al. (1992) wherein the motivation would have been that the computers of Allison et al. (1992) expedite the processing of data (see the second full paragraph on column 1 on page 3977 of Allison et al. (1992)). There would have been a reasonable expectation of success in applying the computational apparatus of Allison et al. (1992) to the empirically derived charge ladders of Carbeck et al. because the article of Allison et al. demonstrates that charge ladders are derivable both computationally and empirically.

35 U.S.C. 103 Rejection #2:

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Carbeck et al. as applied to claims 1-6, 8-9, 12, 15-16, 21-22, and 24 above, and further in view of Greiner et al. [Bioforum, volume 23, 2000, pages 751-754; German article].

Claim 7 is further limiting wherein seven classes are established for the quality label.

Carbeck et al. teaches a method for determining quality value of the biomolecule sample, as discussed above.

Carbeck et al. does not teach use of seven classes.

Greiner et al. studies analysis of biomolecules by lab-on-a-chip technologies.

Specifically, Figure 4 on page 754 of Greiner et al. teaches a protein ladder with seven rungs.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the quality determination method of Carbeck et al. by use of the seven rung ladder of Greiner et al. because it is obvious to substitute known elements in the prior art to yield a predictable result. In this instance, the seven rung ladder is an alternate ladder obtained from electrophoresis than the ladder obtained in Carbeck et al. There would have been a reasonable expectation of success in combining Carbeck et al. and Greiner al. because they pertain to the analogous field of protein charge ladders.

35 U.S.C. 103 Rejection #3:

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Carbeck et al. as applied to claims 1-6, 8-9, 12, 15-16, 21-22, and 24 above, and further in view of Foley [Analytical Chemistry, 1987, volume 59, pages 1984-1987].

Claim 11 is further limiting wherein the geometry of each peak is quantitatively determined.

Carbeck et al. teaches a method for determining quality value of the biomolecule sample, as discussed above.

Carbeck et al. does not teach quantitative determination of peak geometry.

Foley studies quantitative analysis of peak shape and geometry [see title and abstract].

Specifically, Figure 1 on page 1985 of Foley teaches peak geometry analysis.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the quality determination method of Carbeck et al. by use of the peak geometrical analysis of Foley wherein the motivation would have been that quantitative peak shape analysis yields important statistical values in a variety of biological fields (including analytical chemistry which is the field of technology of the protein charge ladders) [see first paragraph of the introduction of Foley].

35 U.S.C. 103 Rejection #4:

Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Carbeck et al. in view of Allison et al. in view of Allison et al. (1992) as applied to claims 1-6, 8-9, 12, 15-16, 21-22, and 24-26 above, and further in view of Walther [Mathematical Methods in the Applied Sciences, 1999, volume 22, pages 301-316].

Claim 13 is further limiting comprising using the rolling ball algorithm.

Carbeck et al., Allison et al., and Allison et al. (1992) make obvious a computational method for determining quality value of the biomolecule sample, as discussed above.

Carbeck et al., Allison et al., and Allison et al. (1992) do not teach use of the rolling ball algorithm to smooth curves.

The article of Walther teaches a generalization of a rolling theorem for the smoothing of surfaces (see title and abstract).

Specifically, Figure 1 on page 1985 of Foley teaches peak geometry analysis.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the empirical quality determination method of Carbeck et al., the computational modeling of Allison et al., and the computational tools of Allison et al. (1992) by use of the rolling ball method of Walther wherein the motivation would have been that smoothing computational generated data makes the data more amenable to in depth mathematical analysis [see abstract and introduction of Walther].

35 U.S.C. 103 Rejection #5:

Claims 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carbeck et al. in view of Allison et al. in view of Allison et al. (1992) as applied to claims 1-6, 8-9, 12, 15-16, 21-22, and 24-26 above, and further in view of Bruneau [J. Chem. Inf. Comput. Sci., 2001, volume 41, pages 1605-1616].

Claim 17 is further limiting wherein a neural network is employed.

Claim 18 is further limiting wherein the neural network encompassed a Bayesian method.

Claim 19 is further limiting wherein the complexity of the functional interrelations is obtainable by iterative additions of hidden neurons to the neuronal network.

Carbeck et al., Allison et al., and Allison et al. (1992) make obvious a computational method for determining quality value of the biomolecule sample, as discussed above.

Carbeck et al., Allison et al., and Allison et al. (1992) do not teach use of neural networks.

The article of Bruneau teaches a search for predictive generic model of aqueous solubility of proteins using Bayesian neural nets [see title and abstract]. This determination of solubility involves calculations of electrostatic properties on the surface of the protein [see Table 2 of Bruneau on page 1608]. The complexity of the interrelations is obtained by iterative additions of hidden nodes in the neural network [see Scheme 1 and last full paragraph on page 1609 of Bruneau].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the empirical quality determination method of Carbeck et al., the computational modeling of Allison et al., and the computational tools of Allison et al. (1992) by use Bayesian neural networks of Bruneau wherein the motivation would have been that these advanced statistical techniques is a comprehensive approach for calculating a wider variety of descriptors in the most attractive and relevant model [see first paragraph in column 1 on page 1606 of Bruneau].

35 U.S.C. 103 Rejection #6:

Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Carbeck et al. in view of Allison et al. in view of Allison et al. (1992) in view of Bruneau as applied to claims 1-6, 8-9, 12, 15-19, 21-22, and 24-26 above, and further in view of Schmidler et al. [Journal of Computational Biology, volume 7, 2000, pages 233-248].

Claim 20 is further limiting wherein the a-posteriori probability of the neuronal network is computed using a Bayesian method.

Carbeck et al., Allison et al., Allison et al. (1992), and Bruneau make obvious a computational method for determining quality value of the biomolecule sample using neural networks and Bayesian methods, as discussed above.

Carbeck et al., Allison et al., Allison et al. (1992), and Bruneau do not teach use of a-posteriori probability analysis.

The article of Schmidler et al. teaches Bayesian segmentation of the protein secondary structure. Specifically, the abstract teaches that posterior probabilities are determined

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the empirical quality determination method of Carbeck et al., the computational modeling of Allison et al., and the computational tools of Allison et al. (1992) and the Bayesian neural networks of Bruneau by use of the a-posteriori probabilities of Schmidler et al. wherein it is obvious to combine known elements in the prior art to yield a predictable result. In this instance using posterior probabilities is an alternate means of conducting the Bayesian analysis than in the prior art of Bruneau (which does not state whether posterior probability analysis was used). There would have been a reasonable expectation of success in combining Carbeck et al., Allison et al., Allison et al. (1992), Bruneau, and Schmidler et al. because all of the studies pertain to statistical analysis of protein electrostatics.

35 U.S.C. 103 Rejection #7:

Claims 21-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carbeck et al. as applied to claims 1-6, 8-9, 12, 15-16, 21-22, and 24 above, and further in view of Goldsborough [WO 00/66605; published 9 November 2000].

Claims 21-22 are further limiting wherein the biomolecules comprise RNA.

Carbeck et al. teaches a method for determining quality value of the biomolecule sample, as discussed above.

Carbeck et al. does not teach use of RNA.

Goldsborough studies various modifications that could be made to nucleotides.

Specifically, Figure 5a of Goldsborough illustrates the schematic for acylation of RNA.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the quality determination method for proteins of Carbeck et al. by use of the acylated RNA of Goldsborough because it is obvious to substitute known elements in the prior art to yield a predictable result. In this instance, the acylation of RNA (instead of proteins) is an alternate means for synthesizing the same charge ladder using a different species of biomolecule. There would have been a reasonable expectation of success in combining Carbeck et al. and Goldsborough because they pertain to the same problem of analyzing acylated biomolecules.

35 U.S.C. 103 Rejection #8:

Claims 10 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carbeck et al. in view of Goldsborough as applied to claims 1-6, 8-9, 12, 15-16, 21-

22, and 24 above, and further in view of Strumberg et al. [Molecular and Cellular Biology, 2000, volume 20, pages 3977-3987].

Claim 10 is further limiting wherein an RNA sample is used involving all eight segments of the RNA.

Claim 14 is further limiting wherein the ratio of areas of the 18S fragment to the 28S fragment is determined.

Carbeck et al. and Goldsborough make obvious a method for determining quality value of an RNA, as discussed above.

Carbeck et al. and Goldsborough do not teach area ratios and specific regions of the RNA.

The article of Strumberg et al. analyzes the structure of certain ribosomal RNA molecules [see introduction of Strumberg et al.] Specifically, Strumberg et al. shows the ratios of the areas of the 18S to the 28S fragment in Figure 1 on page 3978. Additionally, Figure 1 of Strumberg et al. illustrates a schematic of the entire RNA and therefore is interpreted to possess all eight segments recited in instant claim 14.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the RNA quality determination method of Carbeck et al. and Goldsborough by use of the segments of RNA illustrated in Strumberg et al. because it is obvious to substitute known elements in the prior art to yield a predictable result. In this instance, the eight segments of RNA in Strumberg et al. is an alternate means of observing the RNA than the charge ladders of Carbeck et al. applied to the RNA of Goldsborough. There would have been a reasonable expectation of success in

combining Strumberg et al. with the electrostatics and charge ladder of Carbeck et al. and the application of acylations to RNA taught in Goldsborough because all of the studies pertain to electrophoresis of segmented portions of a biomolecule; in Strumberg et al., the observation of the RNA is slightly different that that of Carbeck et al. and Goldsborough (i.e. instead of an electrostatic ladder, the ladder in Strumberg et al. is based on geometric and sequence regions of the RNA). However, there is no limitation requiring that these eight sections of RNA need to be involved in the electrostatic analysis of independent claim 1; to the contrary, claims 10 and 14 only require that the RNA USED have the regions of interest.

35 U.S.C. 103 Rejection #9:

Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Carbeck et al. as applied to claims 1-6, 8-9, 12, 15-16, 21-22, and 24 above, and further in view of Colton et al. [Electrophoresis, 1998, volume 19, pages 367-382].

Claim 23 is further limiting wherein the quality value is a measure of the sample's integrity.

Carbeck et al. teaches a method for determining quality value of the biomolecule sample, as discussed above.

Carbeck et al. does not teach sample integrity.

Colton et al. reviews affinity capillary electrophoresis (i.e. using capillary electrophoresis to measure the affinities of ligands to receptors).

Specifically, Figure 12 on page 381 of Colton et al. uses affinity capillary electrophoresis to measure free energy of binding (i.e. binding affinity or stability) as a function of charge on the receptor. The charge on the receptor is modified to form a charge ladder as described above. It is noted that while integrity is exemplified but not defined on page 1 of the specification, it is interpreted broadly to encompass stability of the bonds between a receptor and a ligand.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the quality determination method for proteins of Carbeck et al. by use of the same charge ladders to measure binding of a receptor to a ligand as in Colton et al. wherein the motivation would have been that the use of the combination of affinity capillary electrophoresis and charge ladders provides an advanced and useful means of quantifying the stability and integrity of a receptor-ligand complex [see introduction of Colton et al. and Figure 12 on page 381 of Colton et al.]

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 8:30 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Marjorie Moran, Supervisory Patent Examiner, can be reached at (571) 272-0720.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Russell S. Negin/
Examiner, AU 1631
7 January 2010